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T-Cell Depleted Allogeneic HSCT for Patients with Relapsed, High-Risk Multiple Myeloma Permits Long-Lasting Remissions in the Absence of Graft-Versus-Host Disease and Provides a Platform for Adoptive Immunotherapeutic Approaches

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Introduction: We planned to reduce early transplant related mortality associated with conventional allogeneic hematopoietic stem cell transplantation (HSCT) and reduce acute or chronic GvHD related to non-myeloablative allo HSCT while maintaining the graft-versus-myeloma effect for patients with high-risk multiple myeloma.

Methods: 34 pts using allo T-cell depleted (TCD) HSCT from HLA compatible (matched related = 12, matched unrelated = 13, and mismatched unrelated = 9) donors. All 34 pts had relapsed myeloma within 15 mos following auto HSCT, and 26/34 pts also had high-risk cytogenetics at diagnosis [t(4;14), t(14;16), del17p by FISH and/or del13q by karyotyping] are reported. All pts had to achieve at least a partial response from salvage chemotherapy (n=26) salvage auto HSCT (n =8). Pts underwent allo TCD HSCT with busulfan (0.8mg/kg x 10 doses), melphalan (70mg/m^2 x 2 days), fludarabine (25mg/m^2 x 5 days) and rabbit ATG (2.5mg/kg x 2 days). T-cell depletion was performed by positive CD34 selection (Isolex) followed by rosetting with sheep erythrocytes for the initial 13pts (2008-09) and by CD34+ enrichment by the Miltenyi Device in 21pts thereafter, achieving $< 10^4$CD3+/kg for all grafts. None of these pts received immuno suppressive therapy post TCD HSCT. Pts were also eligible to receive low doses of donor lymphocyte infusions (DLI) (5x10e^5 – 1x10e^6 CD3+/kg) no earlier than 5mos post allo HSCT.

Results: 34 pts with a median follow up of 33.6mos (range: 9.6 – 67.1 mos) of survivors are reported, median age 56 years (range 32 – 69). TRM and acute GvHD (grade II-IV) at 12mos is 9% (95% CI: 2% – 23%) and 6% (95% CI: 1% – 17%). Chronic GvHD was not observed in any pt. OS and PFS with their 95% CI are shown in Table 1. Factors associated with worse outcome were disease status and number of previous treatments prior to TCD HSCT. 15/34 pts are alive, 10/15 pts are in complete remission (CR), 4 pts are have been in continued CR for 46, 55, 64 and 67mos post allo TCD HSCT. 5/15 pts alive have progressed and 4/5 pts are currently responding to salvage chemotherapy and/or DLI. 14/19pts pts died of disease progression, 3/19 died of infectious complications and 2 pts died of complications associated with acute GvHD.

Conclusion: Long-lasting disease control can be achieved with TCD HSCT in pts with multiply relapsed MM including those with high-risk cytogenetics. TRM and GvHD are low in these heavily pretreated pts. Outcome of TCD HSCT is influenced by numbers of regimens administered and disease status prior to allo BMT.

Table 1

	All patients	3-4 lines of Rx	5-6 lines	> 6 lines
N=	34	13	14	7
CR/nCR	3	3	0	0
VGPR	16	7	7	2
PR	15	3	7	5
PFS @ 1yr (95%CI)	0.49 (0.34 – 0.69)	0.57 (0.36 - 0.90)	0.60 (0.38 - 0.95)	0.0 0.0
PFS @ 2yr (95%CI)	0.27 (0.14 – 0.49)	0.46 (0.24 - 0.86)	0.26 (0.10 - 0.68)	
OS @ 1yr (95%CI)	0.66 (0.51 - 0.85)	0.71 (0.51 - 0.99)	0.75 (0.54 - 0.99)	0.43 (0.18 - 0.99)
OS @ 2yr (95%CI)	0.52 (0.36 - 0.73)	0.71 (0.51 - 0.99)	0.64 (0.41 - 0.99)	0.0

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The Australian Experience with Relapsed Acute Myeloid Leukaemia Post Allogeneic Haematopoietic Stem Cell Transplantation Yields a Simple Prognostic Index for Survival after Relapse

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We retrospectively analysed 386 cases of relapsed acute myeloid leukaemia (AML) from 1336 allogeneic haematopoietic stem cell transplants (alloHSCT) performed between 2000-2011, with two aims: 1. To find and validate factors available at time of relapse that would predict for overall survival from relapse (OS). 2. To determine the effect of first salvage therapy and subsequent GVHD on OS. Aim 1: 349 analysable patients were randomly split into training (n = 233) and validation (n = 116) cohorts. The cohorts were comparable; the only significant difference was more HLA-matched